REMARKS

Applicants thank Examiner Yu for her time during a telephonic interview on June 29, 2004. The undersigned attorney requested that Examiner Yu forward to Applicants the sequence alignment that was referred to in the Office Action mailed March 12, 2004, but which was inadvertently omitted as an attachment to the Action. Applicants thank the Examiner for forwarding a copy of the sequence alignment by facsimile on June 30, 2004.

Favorable reconsideration of the Application is respectfully requested in view of the above amendments and the following remarks. Claims 1-98 are currently pending, and claims 51-58 and 60-63 are being examined on the merits. Applicants hereby cancel non-elected claims 1-50, 59, and 64-98 and claims 52-54 and 60-62 without acquiescence to any rejections and without prejudice to prosecution of this subject matter in any related divisional, continuation, or continuation-in-part application. Claims 51, 55-57, and 63 have been amended to more specifically point out and distinctly claim certain embodiments of Applicants' invention. Support for these amendments may be found throughout the specification and claims as originally filed; Applicants submit that the amendments do not constitute new matter. Support for the amended claims is provided throughout the specification, for example, at page 12, lines 3-14; page 13, line 26 through page 14, line 14; and page 16, lines 10-22. The specification has been amended to correct a typographical error and to conform to recommended citation style for Internet web site addresses. No new matter has been added.

OBJECTION TO THE SPECIFICATION

The PTO objects to the specification, asserting that the paragraph beginning at page 14, line 10 has an embedded hyperlink and/or other form of browser-executable code. The PTO requires removal of the embedded hyperlink and/or other form of browser-executable code at all occurrences in the specification.

Applicants respectfully submit that in view of the amendments to the specification submitted herewith, the basis for this objection has been obviated. In the specification at paragraphs beginning at page 14, line 10; at page 50, line 16; and at page 51, line 17, Applicants have amended the citations referring to an Internet web site pursuant to MPEP § 608.01 and in

conformance with recommended citation style in MPEP § 707.05(e). No new subject matter has been added. Applicants therefore respectfully request that this objection be withdrawn.

CLAIM OBJECTION

The PTO objects to claims 55-58 for lack of formality, asserting that the claims depend from a withdrawn claim. The PTO requires correction of the informality.

Applicants submit that in view of the amendments submitted herewith, which include amendments to claim 55 that remove dependency on cancelled claim 50, claims 55-58 meet the formality requirements. Applicants therefore respectfully request that this objection be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (WRITTEN DESCRIPTION)

The PTO rejects claims 55, 57, 58, and 60-64 under 35 U.S.C. § 112, first paragraph, asserting that the claims are directed to subject matter that is not adequately described in the specification. More specifically, the PTO asserts that in the absence of distinguishing, identifying, functional characteristics, the specification does not provide adequate written description of a genus of polynucleotides that encode a polypeptide having at least 50% identity to SEQ ID NO:21 or a genus of polynucleotides that hybridize under the recited conditions to SEQ ID NO:20.

Applicants respectfully traverse this rejection and submit that Applicants possessed the claimed invention, as disclosed in the present specification and recited in the instant claims, at the time the Application was filed. Applicants submit that in view of the amendments submitted herewith, which include cancellation of claims 60-62 without acquiescence to any rejection or prejudice to prosecution of this subject matter in a related application, the rejection of these claims is rendered moot.

As described in the specification and recited in the instant claims, the invention is directed in pertinent part to an isolated polynucleotide that encodes a polypeptide capable of dephosphorylating an activated mitogen-activated protein kinase (MAP-kinase), wherein the polynucleotide comprises a sequence at least 90% identical to SEQ ID NO:20, and wherein the

encoded polypeptide comprises an amino acid sequence VHCLAGISRS (SEQ ID NO:16), and to related compositions and methods.

The specification provides a detailed description of relevant and identifying characteristics of the claimed genus that reasonably conveys to a person skilled in the art that Applicants possessed more than a single representative species. The instant Application discloses a polynucleotide sequence (SEQ ID NO:20) encoding a DSP-16 alternate form polypeptide (SEQ ID NO:21), thus providing a detailed, structural chemical formula from which a skilled person may routinely make and use the claimed polynucleotides. As described in the specification, polynucleotides encoding DSP-16 alternate form polypeptide may comprise a native sequence or a variant of such a sequence (*see, e.g.*, page 13, line 26 through page 14, line 14). Polynucleotide variants may occur as a result of the degeneracy of the genetic code (page 14, line 28 through page 15, line 4), which comprises triplet codons having nucleotide sequences that are well known and conventional to persons skilled in the molecular biology art.

The specification also describes a polynucleotide that encodes a DSP-16 alternate form polypeptide variant capable of dephosphorylating an activated MAP-kinase, wherein the polynucleotide comprises a sequence at least 90% identical to a polynucleotide comprising the nucleotide sequence set forth in SEQ ID NO:20 (*see, e.g.*, page 12, lines 3-19; page 13, line 26 through page 14, line 14). As recited in the instant claims and described in the specification, the ability of the encoded DSP-16 alternate form variant to dephosphorylate tyrosine and serine/threonine residues within a DSP-16 alternate form substrate is not substantially diminished relative to native DSP-16 alternate form polypeptide (*see, e.g.*, page 10, lines 11-20; page 12, lines 3-19; page 21, line 14 through page 22, line 14).

Moreover, the specification describes the structural features of the claimed subject matter that correlate with functional activity. Specifically, the protein tyrosine phosphatase active site domain comprising the sequence VHCLAGISRS (SEQ ID NO:16) within the DSP-16 alternate form polypeptide sequence (*see* positions 94-103 of SEQ ID NO:21) is encoded by the claimed polynucleotides (*see, e.g.*, page 12, lines 3-14; page 16, lines 10-22; page 50, lines 7-15, and references therein; SEQ ID NO:21). On the basis of the disclosure in the specification, a skilled artisan would appreciate that a DSP-16 alternate form variant polypeptide encoded by the claimed polynucleotides preferably contains conservative substitutions such that the catalytic

activity of the variant is not substantially changed (*see, e.g.,* page 11, lines 18-22). The specification also describes how the catalytic activity of the enzyme may be disabled if the cysteine residue within SEQ ID NO:16, which is located at position 96 in SEQ ID NO:21, and/or the aspartate residue that is located N-terminal to the active site motif (position 65 of SEQ ID NO:21) are substituted (*see, e.g.,* page 10, line 21 through page 11, line 17, which describe the corresponding positions in a DSP-16 polypeptide (SEQ ID NO:2)). Therefore, and as described in the specification, a polynucleotide that encodes a DSP-16 alternate form polypeptide variant capable of dephosphorylating an activated MAP-kinase preferably retains these cysteine and aspartate residues. Applicants submit that therefore a person skilled in the art would readily be able to identify the species encompassed by the instant claims, given the recited *structural* features of DSP-16 alternate form sequences and amino acid sequence position numbers, *and* the recited *functional* feature that the DSP-16 alternate form polypeptide retains the ability to dephosphorylate an activated MAP kinase.

Accordingly, Applicants submit that the claimed subject matter is adequately described by the specification such that a person skilled in the art would recognize that Applicants possessed the claimed invention at the time the Application was filed. Applicants therefore submit that the Application complies with the written description requirement under 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection be withdrawn.

REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH (ENABLEMENT)

The PTO rejects claims 51-58 and 60-63 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. The PTO concedes that the specification enables the polynucleotide sequence, SEQ ID NO:20, which encodes the full-length protein of SEQ ID NO:21; however, the PTO alleges that the specification does not reasonably provide enablement for any polynucleotide encoding a fragment or a mutant of the polypeptide.

Applicants respectfully traverse this rejection and submit that as disclosed in the present specification and recited in the instant claims, Applicants fully enabled the claimed invention at the time the Application was filed. Applicants submit that in view of the

amendments submitted herewith, which include cancellation of claims 52-54 and 60-62 without acquiescence or prejudice, the rejection of these claims is rendered moot.

Applicants submit that the disclosure provides enabling guidance for a person skilled in the art to make and use the claimed polynucleotides encoding a DSP-16 alternate form polypeptide readily and without undue experimentation. As conceded by the PTO, the specification is enabling for a polynucleotide sequence (SEQ ID NO:20) that encodes a DSP-16 alternate form polypeptide (SEQ ID NO:21) that is capable of dephosphorylating a DSP-16 alternate form substrate, for example, an activated MAP-kinase (*see, e.g.,* page 10, lines 4-11). As taught in the specification, DSP-16 alternate form encoding polynucleotides may comprise a native sequence or a variant of such a sequence (*see, e.g.,* page 13, line 26 through page 14, line 10). Such polynucleotide variants may occur as a result of the degeneracy of the genetic code (page 14, line 28 through page 15, line 4), which is well known and routinely used by persons skilled in the molecular biology art. The specification further describes how to make and use an isolated polynucleotide that encodes a DSP-16 alternate form polypeptide variant capable of dephosphorylating an activated MAP-kinase, wherein the polynucleotide comprises a nucleotide sequence at least 90% identical to SEQ ID NO:20 (*e.g.,* page 9, line 23 through page 10, line 2; page 10 , lines 4-20; page 13, line 26 through page 14, line 10). By using computer algorithms well known in the art and disclosed in the specification, such as Align or the BLAST algorithm, a person skilled in the art can determine the percentage of nucleotide sequence identity shared by a candidate polynucleotide sequence with the DSP-16 alternate form polynucleotide sequence disclosed in the instant application (*see, e.g.,* page 14, lines 6-11).

The specification also describes DSP-16 alternate form amino acid residues and polypeptide regions, which, if changed, result in compromised phosphatase activity. That is, the specification describes the location and identity in a DSP-16 alternate form polypeptide of amino acids that contribute to DSP-16 alternate form catalytic dephosphorylation activity, and which therefore are not amenable to modification in the design of a polynucleotide encoding a functional (*i.e.,* catalytically active) DSP-16 alternate form variant. Specifically, the DSP-16 alternate form polypeptide encoded by the claimed polynucleotide belongs to the family of protein tyrosine phosphatases that share a conserved catalytic domain containing a cysteine residue situated N-terminal to a stretch of five variable amino acids followed by an arginine

residue (*see, e.g.,* page 50, lines 7-13, and references therein). For determining that a polynucleotide encodes a DSP-16 alternate form polypeptide that retains the ability to dephosphorylate an activated MAP-kinase, the specification teaches that the DSP-16 alternate form active site domain comprises the sequence VHCLAGISRS (SEQ ID NO:16), which is located at positions 94-103 of SEQ ID NO:21 (*see, e.g.,* page 12, lines 3-14; page 16, lines 10-22; SEQ ID NO:21). The specification also describes the relationship between wildtype aspartate at position 65 of SEQ ID NO:21 (which corresponds to position 213 in SEQ ID NO:2 (DSP-16)) and catalytic phosphatase activity, for example, through the use of substrate trapping mutants of DSP-16 alternate form (*see, e.g.,* page 10, line 21 through page 11, line 17, and references cited therein). Thus, clearly, given the DSP-16 alternate form polynucleotide sequence and the locations within the encoded polypeptide sequence of the amino acids comprising the catalytic active site, a skilled artisan, using alignment methods as discussed above, would be able to identify readily and routinely whether a polynucleotide contains sequences that encode a catalytically active DSP-16 alternate form polypeptide.

Given such description in the specification, the person skilled in the art may reasonably and rationally predict that modifications not affecting catalytic activity may be made to residues that are not implicated in catalytic activity. According to textbook knowledge in the molecular biology arts with respect to enzymes, "[in] fact, evidence now indicates that amino acid replacements in many parts of a polypeptide chain can occur without seriously modifying catalytic activity" *(see Molecular Biology of the Gene*, page 227 (James D. Watson et al., ed., The Benjamin/Cummings Publishing Co., (Menlo Park, CA) (4th ed. 1987)). Particularly, as taught in the specification and understood in the art, a skilled artisan would expect that the secondary structure and hydropathic nature of the DSP-16 alternate form polypeptide would be substantially unchanged if a conservative amino acid substitution were made to such residues, that is, conservative modifications would be tolerated (*see, e.g.,* specification at page 11, lines 18-24). The specification also provides an alignment of several dual specificity phosphatases, which alignment of related sequences, as discussed at length by Bowie et al. (*Science* 247:1306-10, 1308-309 (1990)), is useful for analyzing determinants of protein folding, stability, and protein function.

Furthermore, a person skilled in the art would be able to identify or make a DSP-16 alternate form polypeptide, or a variant thereof, that retains the ability to dephosphorylate a DSP-16 alternate form substrate, according to methods known in the art and disclosed in the specification without undue experimentation (*see, e.g.,* page 21, line 14 through page 23, line 11). A skilled artisan can identify such a DSP-16 alternate form polypeptide by expressing it using the presently claimed polynucleotide (*see, e.g.,* page 12, line 20 through page 13, line 13; page 19, lines 4-12; page 20, line 1-28; *see also* page 37, line 26 through page 40, line 7). The polypeptide so produced can then be routinely analyzed for its ability to dephosphorylate a suitable DSP-16 alternate form substrate according to assays for detecting DSP-16 alternate form activity, which are also described in the specification (*see, e.g.,* pages 21-23). Applicants respectfully submit that given the teachings of the present specification and, *inter alia*, the level of skill in the art, performing such assays to determine whether an encoded DSP-16 alternate form polypeptide has MAP-kinase phosphatase activity would not amount to undue experimentation, but instead is merely a matter of permissible routine screening. (*See In re Wands*, 858 F.2d 731, 736, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) ("Enablement is not precluded by the necessity for some experimentation such as routine screening.")).

Accordingly, Applicants respectfully submit that the requirements for enablement under 35 U.S.C. § 112, first paragraph, are met and request that this rejection be withdrawn.

REJECTION UNDER U.S.C. §102(e)

The PTO rejects claims 51-55, 57, 58, and 60-63 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,664,089 (Meyers). In particular, the PTO asserts that SEQ ID NO:1 described in Meyers is 88.5% identical to SEQ ID NO:20 and 94.4% identical to a polynucleotide encoding the polypeptide of SEQ ID NO:21 in the present Application. The PTO also alleges that SEQ ID NO:3 described in Meyers is 94.4% identical to a polynucleotide encoding SEQ ID NO:21. Further, the PTO asserts that Meyers teaches an expression vector, a host cell, and a method of producing protein.

Applicants respectfully traverse this ground of rejection and submit that Meyers fails to teach or suggest each and every limitation of the instant claims and therefore does not destroy the novelty of the claimed invention. Applicants submit that the rejection of claims 52-

54 and 60-62 is rendered moot in view of the amendments submitted herewith, which include cancellation of these claims without acquiescence or prejudice.

Meyers fails to teach or suggest an isolated polynucleotide that comprises a nucleotide sequence at least 90% identical to SEQ ID NO:20 and that encodes a DSP-16 alternate form polypeptide capable of dephosphorylating an activated MAP-kinase, wherein the polypeptide comprises an amino acid sequence VHCLAGISRS (SEQ ID NO:16). Meyers also fails to teach or suggest an expression vector that comprises such a polynucleotide, and also fails to teach or suggest a host cell comprising the expression vector or a method for producing the DSP-16 alternate form polypeptide using the host cell.

Accordingly, Applicants respectfully submit that the claimed subject matter satisfies the novelty requirements under 35 U.S.C. § 102 and request that the rejection be withdrawn.

Applicants respectfully submit that all claims in the Application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

Mae Joanne Rosok
Registration No. 48,903

MJR:jjf

701 Fifth Avenue, Suite 6300
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

491122